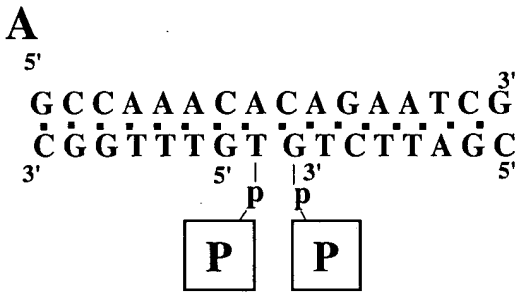
AMENDMENTS TO THE SPECIFICATION:

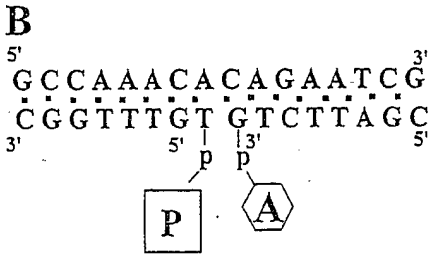
Please amend the paragraphs beginning at page 20, line 1, as follows:

Comparative) SP-1: (excimer split-probe system) (SEQ ID NOs:1-3, respectively)



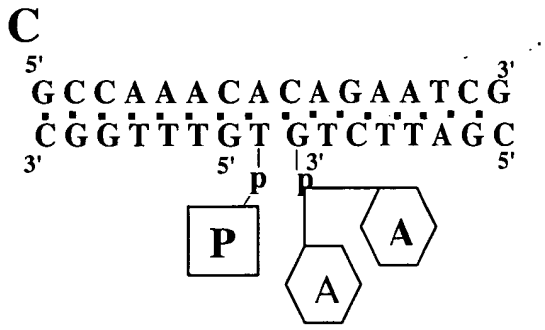
where: **P** is a Pyren-1-yl-methylamino group and **p** is a phosphate group connecting P to the backbone of the probe (see also the structural formula in Fig 1).

SP-19 (exciplex split-probe system): SEQ ID NOs:1-3, respectively)

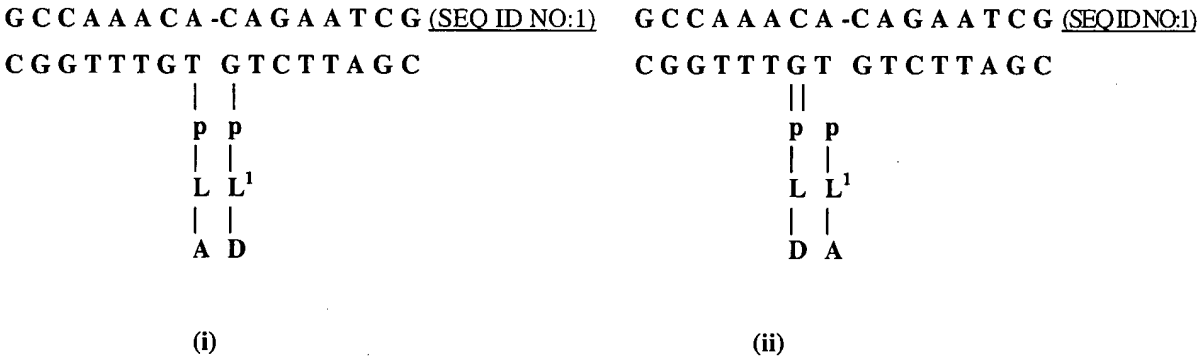


where: **A** is a 2-(N'-methyl-N'-naphth-1"ylamino) ethylamino group, **P** is a pyren-1-yl-methylamino group and **p** is a phosphate group connecting P or A to the backbone of the probe (see also the structural formula in Fig 1).

SP-34 (exciplex split-probe system): (SEQ ID NOs:1-3, respectively)



Please amend the paragraphs beginning at page 26, line 8, as follows:



Please amend the paragraphs beginning at page 29, line 5, as follows:

Two 8-mer probes were used to complement a 16-mer parent RNA sequence as shown below, the sequences being chosen so that they were not self complementary, only bound to the parent RNA sequence in the way required, and were not able to overlap (SEQ ID NOs:4, 2 and 5, respectively).

G-C-C-A-A-A-C-A-C-A-G-A-A-U-C-G RNA target strand

C-G-G-T-T-T-G-T G-A-C-T-T-A-G-C

A B

Please amend the paragraphs beginning at page 32, line 1, as follows:

Nomenclature **Target sequence**

Parent (SP19) (SEQ ID NOs:1-3, respectively)

GCCAAACA-CAGAATCG

CGGTTTGT GTCTTAGC

A B

Insertion 1 (SEQ ID NOs:6, 2 and 3, respectively)

GCCAAACAGCAGAATCG

CGGTTTGT GTCTTAGC

A B

Insertion2 (SEQ ID NOs:7, 2 and 3, respectively)

GCCAAACAGTCAGAATCG

CGGTTTGT GTCTTAGC

A B

3'mismatch 1 (SEQ ID NOs:8, 2 and 3, respectively)

GCCAAACA-CAGAATAG
CGGTTTGT GTCTTAGC
A B

3'mismatch 2 (SEQ ID NOs:9, 2 and 3, respectively)

GCCAAACA–CAGGATCG
CGGTTTGT GTCTTAGC
A B

3'-mismatch 3 (SEQ ID NOs:10, 2 and 3, respectively)

GCCAAACA-AAGAATCG
CGGTTTGT GTCTTAGC
A B

3'-double mismatch (SEQ ID NOs:11, 2 and 3, respectively)

GCCAAACA-CAGGATGG
CGGTTTGT GTCTTAGC
A B

Please amend the paragraphs beginning at page 33, line 1, as follows:

5'-mismatch 1 (SEQ ID NOs:12, 2 and 3, respectively)

GACAAACA-CAGAATCG
CGGTTTGT GTCTTAGC
A B

5'-mismatch 2 (SEQ ID NOs:13, 2 and 3, respectively)

GCCAGACA-CAGAATCG
CGGTTTGT GTCTTAGC
A B

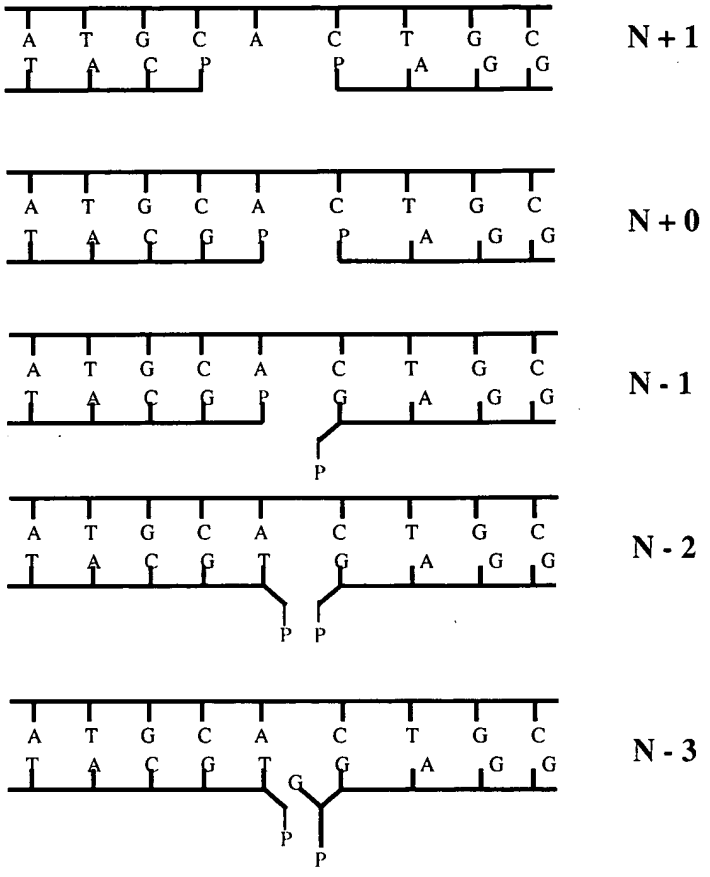
5'-mismatch 3 (SEQ ID NOs:14, 2 and 3, respectively)

GCCAAACT-CAGAATCG
CGGTTTGT GTCTTAGC
A B

5'-double mismatch (SEQ ID NOs:15, 2 and 3, respectively)

GACAGACA-CAGAATCG
CGGTTTGT GTCTTAGC
A B

Please amend the paragraphs beginning at page 39, line 1, as follows:



N + 1 (SEQ ID NOs:16-18, respectively), N + 0 (SEQ ID NOs:16, 19 and 18, respectively), N – 1 (SEQ ID NOs:16, 19 and 20, respectively), N – 2 (SEQ ID NOs:16, 21 and 20, respectively), and N – 3 (SEQ ID NOs:16, 21 and 22, respectively).

Please amend the paragraphs beginning at page 45, line 4, as follows:

The construct investigated was based on the SP-19 system but in which the probes were as follows:

Pyrene-5'-p-TGT^{L}T^{L}T^{L}GGC (SEQ ID NO:23)
CGATTGGC-3' (SEQ ID NO:24) -p-Naphthalene

Spectra were recorded in Tris Buffer/80% TFE at 10°C. The Tris Buffer contained 0.1M NaCl, 10mM Tris, pH 8.3. Concentration of oligonucleotide components was 2.5 μM for all oligonucleotides.

The results are shown in Figure 32.

This figure shows the strong exciplex fluorescence at approx 490 nm from the perfect complement of the target used for SP-19 in the DNA studies described in Example 1 above (the probe oligos here had 3 LNA residues as indicated in the pyrene-bearing probe oligo, shown as T^L). In comparison with use of a fully DNA-based probe oligo the exciplex fluorescence intensity is greater for this $SL^3$19 LNA-based oligo probe.

The above procedure was repeated but by introducing a mismatch into the oligo probe containing LNA. The probes used for this investigation are shown below:

Pyrene-5'-p-TGC^{L}T^{L}T^{L}GGC (SEQ ID NO:25)
CGATTGGC-3' (SEQ ID NO:24)-p-Naphthalene

Please amend the paragraphs beginning at page 47, line 6, as follows:

N'-methyl-N'-naphthalen-1-yl-ethane-1, 2-diamine was attached via a phosphoramidate link to the terminal 5'-phosphate of ON1 (5'pTGTTTGGC) (SEQ ID NO:23) and the 3'-phosphate of ON2 (CGATTCTG3'p) (SEQ ID NO:26) by the procedure described, but using N'-methyl-N'-naphthalen-1-yl-ethane-1, 2-diamine dihydrochloride (2 mg, 7.3 μmol dissolved in 100 μl of DMF and 3μl triethylamine). The product was purified by reverse-phase HPLC (eluted by 0.5 M $LiClO_4$ with a gradient from 0 to 40 % acetonitrile). Products were identified by UV/

visible spectroscopy and appropriate fractions were lyophilised. Typical yields were around 80%. The UV/visible absorption spectra of unmodified ON1 and ON1-5'Np are shown in Figure 28. The shoulder at 310 nm on the 260 nm absorption band indicates the presence of naphthalene.

Bis-attachment of N'-Methyl-N'-naphthalen-1-yl-ethane-1,2-diamine dihydrochloride to oligonucleotide probes.

Two equivalents of N'-methyl-N'-naphthalen-1-yl-ethane-1,2-diamine dihydrochloride were attached via phosphoramidate links to the terminal 5'-phosphate of ON1 (5'pTGTTTGGC) (SEQ ID NO:23) or to the 3'-phosphate of ON2 (CGATTCTG3'p) (SEQ ID NO:26) to the cetyltrimethylammonium salts of the oligonucleotides (~1μmol) dissolved in DMF (200 μl) were added triphenylphosphine (80 mg, 300 μmol) and 2',2'-dipyridyl disulfide (70 mg, 318 μmol), and the reaction mixture incubated at 37 °C for 10 min. 4-*N',N'*-Dimethylaminopyridine (40 mg, 329 μmol) was then added and the reaction mixture incubated for a further 10 minutes at 37 °C. N'-Methyl-N'-naphthalen-1-yl-ethane-1,2-diamine dihydrochloride (4 mg, 14.6 μmol, dissolved in 100 μl of DMF and 3μl triethylamine) was added. The reaction mixture was incubated at 50 °C for 24 hours, precipitated as described above and purified using reverse-phase HPLC (eluted by an aqueous solution of 0.05 M $LiClO_4$ with a gradient from 0 to 60 % acetonitrile). Products were identified by UV/ visible spectroscopy and appropriate fractions were lyophilised.

Before the Figures, insert the Sequence Listing submitted herewith.